Influence of knee joint angle on muscle properties of paralyzed and nonparalyzed human knee extensors

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ABSTRACT: Muscles of individuals with a spinal cord injury (SCI) exhibit an unexpected leftward shift in the force (torque)–frequency relationship. We investigated whether differences in torque–angle relationships between SCI and able-bodied control muscles could explain this shift. Electrically stimulated knee-extensor contractions were obtained at knee flexion angles of between 30° and 90°. Torque–frequency relationships were obtained at 30°, 90°, and optimum angle. Optimum angle was not different between groups but SCI-normalized torques were lower at the extreme angles. At all angles, SCI muscles produced higher relative torques at low stimulation frequencies. Thus, there was no evidence of a consistent change in the length of paralyzed SCI muscles, and the anomalous leftward shift in the torque–frequency relationship was not the result of testing the muscle at a relatively long length. The results provide valuable information about muscle changes occurring in various neurological disorders.

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INFLUENCE OF KNEE JOINT ANGLE ON MUSCLE PROPERTIES OF PARALYZED AND NONPARALYZED HUMAN KNEE EXTENSORS

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A great deal of information has been obtained in recent years concerning muscle adaptations after spinal cord injury (SCI). Below the level of a complete lesion, muscles cannot be activated voluntarily and this leads to a loss of muscle mass[5,6,34] and oxidative capacity[11,19,25] and a reduction in the proportion of slow muscle fibers,[3,4,11,28] which are associated with muscle weakness, rapid fatigability, and increased contractile speed.[10,26,30–32] In addition, the relationship between force-generating capacity and stimulation frequency is altered after SCI in a way that is unexpected for muscles that have changed into being composed of predominantly fast (type 2) muscle fibers. The relationship between stimulation frequency and force production is typically a sigmoidal curve[8] that differs between fast and slow muscles. Higher stimulation frequencies are required in fast muscles to obtain the same level of force production relative to maximum force as seen in slow muscles.[7,16] The curve is said to be shifted to the left for slow muscles and to the right for fast muscles. The paralyzed muscles of SCI patients are typically composed of type 2 fibers that can be demonstrated to be fast in type by their histochemical staining, the rate of relaxation from a stimulated contraction, and the extent of force oscillation during an unfused tetanus. Nevertheless, the force–frequency relationship is found to be shifted to the left, a feature that is normally associated with a slowing of contractile properties.[10,26] No explanation has been found for this phenomenon, which appears to be associated with an abnormally large twitch force and is largely normalized as a result of training with electrical stimulation.

The force generated by a muscle depends on the length of its contractile elements. This is evident for a muscle such as the quadriceps in the in vivo relationship between maximum torque and joint angle.[12,15,23] This force–length relationship is also af-

Abbreviations: ANOVA, analysis of variance; pQCT, peripheral quantitative computed tomography; MVC, maximum voluntary contraction; SCI, spinal cord injury
Key words: isometric contraction; muscle length; muscle torque; quadriceps; spinal cord injury
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fected by the stimulation frequency so that, with increasing frequency, the optimum muscle length is shifted to shorter lengths.[24] The force–frequency relationship shifts to higher frequencies, or to the right, with shorter muscle lengths,[9,27] and to the left when muscles fibers are tested at a longer length. In a number of pathologic conditions (e.g., after a stroke) or with certain neuromuscular diseases (e.g., nemaline myopathy), there is a change in the torque–angle relationship,[1,12] suggestive of shorter muscle lengths. Likewise, immobilization in a shortened position has been shown to lead to a shift in the optimum length to smaller angles of knee flexion.[35] It is likely, therefore, that the torque–angle relation of the knee-extensors of individuals with SCI is also shifted toward more knee extension (shorter muscle length). Our previous observations of a leftward shift of the force–frequency relationship in SCI was made with the knee of normal and SCI subjects at 90° and it is therefore possible that the SCI muscles were tested at a relatively longer length in the patients than in controls. This in turn might explain the unexpected differences in the force–frequency relationships.

The purpose of this study was to investigate differences in the torque–angle relationships of knee-extensor muscles of SCI and able-bodied subjects and to determine whether differences in the torque–frequency relationship between groups could be explained by any such differences.

METHODS

Subjects. The present study included six men with SCI (age 36 ± 5 years) and eight age-matched, able-bodied control subjects (men, aged 37 ± 4 years). Values for body mass and height were 81 ± 6 kg and 1.87 ± 0.03 m for SCI subjects and 78 ± 3 kg and 1.83 ± 0.02 m for the controls. In three SCI subjects, the lesion level was at C-5, in two at T-7, in one at T-11, and in one at L-1. The lesion duration varied from 1.5 to 24 years. In five subjects, the spinal lesion was complete, in one it was sensory incomplete, and in one the lesion was both sensory and motor incomplete but without functional motor activity (American Spinal Injury Association score,[20] A–C). Spinal reflexes were present in all SCI subjects. None of the subjects had a previous history of neurological (other than SCI), cardiovascular, or musculoskeletal problems. Furthermore, subjects were examined by an experienced physician with peripheral quantitative computed tomography (pQCT) using an XCT2000 scanner (StraTec, Pforzheim, Germany) to ensure they had no serious osteoporotic problems of the lower limbs. None of the SCI subjects had participated in electrical stimulation training programs specific for the lower-limb muscles, and the control subjects were all moderately active. All subjects signed written informed consent after careful explanation about testing procedures and the risks involved. The medical ethics committee of the Vrije University Medical Centre, Amsterdam, approved the study.

Experimental Procedure. All subjects participated in one experimental session with assessment of electrically stimulated contractile properties of the knee-extensor muscles of the right leg. Subjects were asked to refrain from strenuous exercise 48 hours prior to the experiments. Before the start of the experiments subjects were familiarized with the test procedures. Isometric knee-extension torques were obtained at different knee-flexion angles with the subjects seated on a custom-built, computer-controlled, lower-limb dynamometer. The pelvis and upper body were fixed securely to the seat, with the hip flexed at approximately 70°, to minimize movements other than knee extension, and the subject's shin was connected to the lever arm of the dynamometer. At each joint angle, care was taken so that the axis of the lever arm was always aligned with the axis of the knee joint (lateral femoral condyle).

Torques (0.001-Nm resolution) were measured at the motor axis and are therefore independent of the length of the lever arm. Torque signals were digitized (1000 Hz) and stored on disk for off-line analysis.

For reasons of safety of the SCI subjects, the lever arm could be disconnected, either by the investigator or subject, via a safety button; this was to prevent any damage in the event of, for instance, a severe muscle spasm. Furthermore, the maximum knee-extension torque allowed to be produced by the SCI subjects was set at 75 Nm, in which case the lever arm would begin to move, allowing the knee to extend. In the testing, this maximum torque was never reached by any of the SCI subjects.

Electrical Stimulation. For the assessment of contractile properties, two different stimulation strategies were used. Torque–angle relationships were obtained by activating the quadriceps maximally with surface stimulation of the femoral nerve. For this purpose, two self-adhesive electrodes (Schwa-Medico BV, Nieuw Leusden, The Netherlands) were used, the cathode in the femoral triangle over the femoral nerve (5 × 5 cm) and the anode (8 × 13 cm) distally over the medial part of the quadriceps muscle. Percutaneous muscle stimulation was used for the assessment of torque–frequency relationships. A distal electrode (both 8 × 13 cm) was placed over the medial part of the quadriceps muscle with the proximal electrode over the lateral portion of the muscle. A constant-current electrical stimulator (Model DS7A; Digitimer, Ltd., Welwyn Garden City, UK) delivered the square-wave electrical pulses (0.2-ms duration) to the quadriceps muscle. A personal computer controlled the number and frequency of the electrical pulses delivered.

Protocol. Knee-extensor torque responses were obtained at seven randomly assigned knee-flexion angles ranging between 30° and 90° knee flexion, with 10° intervals (0° corresponding to full knee extension). For this purpose, 3 pulses at 300 Hz (a triplet) were imposed on the femoral nerve with the current intensity set at a supramaximal level such that no further torque increase was observed. The triplet was used instead of a full tetanus because the production of high knee-extensor torques is undesirable in SCI subjects due to the risk of bone fractures.[13]

To assess whether torque–angle relationships obtained using triplet stimulation provided similar information to the maximum voluntary efforts, pilot experiments were performed in a selected group of able-bodied subjects ($n = 5$). Torque–angle relationships were obtained with maximal voluntary contractions (MVCs) and compared with those from supramaximal triplets. Subjects were asked to perform MVCs of approximately 4–5 s at each angle, separated by 2-min rest. During each voluntary effort, subjects were loudly encouraged and visual feedback was provided.

For assessment of the torque–frequency relationship, the knee-extensors were activated with the muscle surface stimulation technique, and current intensity was reduced such that the triplets evoked with such stimulation were approximately 50% of the maximum triplet torque obtained with nerve stimulation. Subsequently, series of stimulus trains (700 ms) at 10, 20, 50, and 150 Hz were evoked at 90° and 30° knee flexion and at the optimum angle determined from the torque–angle relationship for each subject. Stimulus trains were separated by 2-min rest.

Data Analysis. Torque recordings were analyzed off-line using customized software (Matlab, The Mathworks, Natick, Massachusetts). Torque–angle curves were obtained from the peak triplet torque at each knee-flexion angle. Whereas the individual curves from the controls could be well fitted by a second-order polynomial, this was not possible for the SCI subjects.

Therefore, the angle corresponding to the peak triplet torque from the individual torque–angle relationship was taken for comparison between groups rather than an estimate of the optimum from a fitted curve. To compare the range of active torque production between subjects, relative torque–angle relationships were estimated. For this purpose, the optimum joint angle was defined as 0° and normalized torques (degrees of deviation from optimum angle) were calculated from the individual fitted curves at 10° intervals, between −30° and +30°. Torque–frequency relationships were obtained from peak torques at each stimulation frequency. Twitch torque was calculated using the torque response of the first pulse in a 10-Hz torque signal.

Statistical Analysis. To determine whether there were any differences in torque production with varying joint angle between SCI and control subjects, repeated-measures, mixed-design, factorial analyses of variance (ANOVAs) were performed and the interaction between group and angle was examined. Student's t-tests were performed to test for differences between experimental groups for the optimal knee-flexion angle. Two-factor (stimulation frequency × knee-flexion angle) repeated-measures ANOVA was used to test for differences between experimental groups with stimulation frequency, knee-flexion angle, and their interaction on torque production. Post hoc simple contrast analysis was used to study differences between repeated measures. All data are presented as mean ± SEM unless otherwise indicated, and levels of significance were set at $P < 0.05$.

RESULTS

Relationship of Maximal Torque to Knee-Flexion Angle. To minimize the risk of damage to osteoporotic bones, we used triplet stimulation rather than maximal contractions to define the length–torque relationships of control and SCI muscles. Figure 1 shows that, for the control subjects, triplet stimulation identified the same optimum knee angle for torque generation as maximal voluntary contractions. We assumed, therefore, that triplet stimulation also reliably defines the optimum angle in SCI subjects.

Maximal triplet torque of the knee-extensors (Fig. 2A) was significantly lower at all knee-flexion angles in the SCI subjects than control subjects ($P < 0.001$). Peak torque was 40 ± 5 Nm and 107 ± 5 Nm in SCI and control subjects, respectively. Averaged

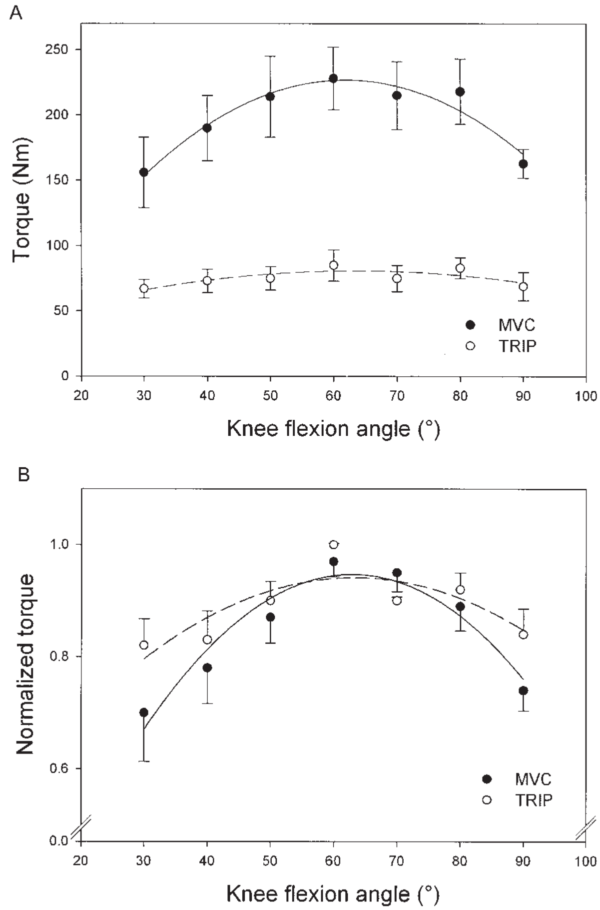

FIGURE 1. Torque–angle relationships obtained with triplet (TRIP) stimulation and maximum voluntary contractions (MVC) in five able-bodied control subjects. **(A)** Average absolute torque responses. **(B)** Torque responses normalized for peak torque. Error bars represent SEM.

over all angles, SCI torques were 35% of those in controls.

To compare curves of subjects with different strength, individual data were normalized by expressing the torque data at each knee-flexion angle relative to optimum angle (Fig. 2C,D). The variation of torque–angle relationships between SCI subjects (Fig. 2C) was much greater than between controls (Fig. 2D). The individual curves of the controls, but not the SCI subjects, could be fitted well by a second-order polynomial. For this reason, the angle corresponding to the peak triplet torque from the individual torque–angle relationship was taken for comparison between groups rather than an estimate of the optimum from a fitted curve. The mean optimum joint angle was 66 ± 5° in SCI subjects and 67 ± 6° in controls, which was not a statistically significant difference between groups.

To examine the active range of torque production, the data were rescaled such that torque responses relative to maximum were plotted against the joint angle relative to optimum (Fig. 2B). The variation of torque with knee angle differed between the groups ($P < 0.05$). The knee-extensors of SCI subjects were relatively weak in their shortened and lengthened positions compared to those of control subjects, so that, at 30° less than optimum angle, SCI muscles produced approximately 70% of peak torque compared to 85% in control muscles; at 30° greater than optimum, this was approximately 75% compared to 85% for controls. This torque reduction at the extreme knee angles in the SCI group is consistent with a smaller active working range of the muscle fibers due to a reduced fiber length.

Torque–Frequency Relationship. Torque–frequency curves of the knee-extensors for the SCI and control groups are shown in Figure 3. At all angles, torque responses of the SCI subjects were significantly reduced ($P < 0.01$) compared to controls for all stimulation frequencies except for the twitch.

To compare the influence of activation frequency on torque production between groups, irrespective of maximal strength, individual torque–frequency curves were normalized by expressing the data relative to peak (150-Hz) torque. There was a clear effect of joint angle on the torque–frequency relationship (Fig. 4) with a shift toward lower stimulation frequencies with greater knee flexion, that is, longer muscle lengths ($P < 0.01$). This effect was present in both SCI and controls, but was more marked for the SCI subjects, where the difference in twitch force varied threefold between short and long muscle lengths (Fig. 4B), as opposed to twofold for the control muscles (Fig. 2A). At all joint angles, the SCI subjects developed greater torque at lower frequencies than controls (Fig. 5). For example, at the optimum angle, relative twitch torques were 0.34 ± 0.05 in SCI subjects and 0.11 ± 0.01 in controls ($P < 0.01$).

DISCUSSION

The major effects of SCI on muscle bulk and fiber type composition are well documented, but the anomalous shift in the force–frequency relationship is unexplained. Despite the fact that SCI muscle generally has faster contractile properties than control muscle, the force–frequency relationship is shifted to the left, primarily because of very large twitch forces. Although the maximum tetanic force of SCI muscle may be about one third that of a

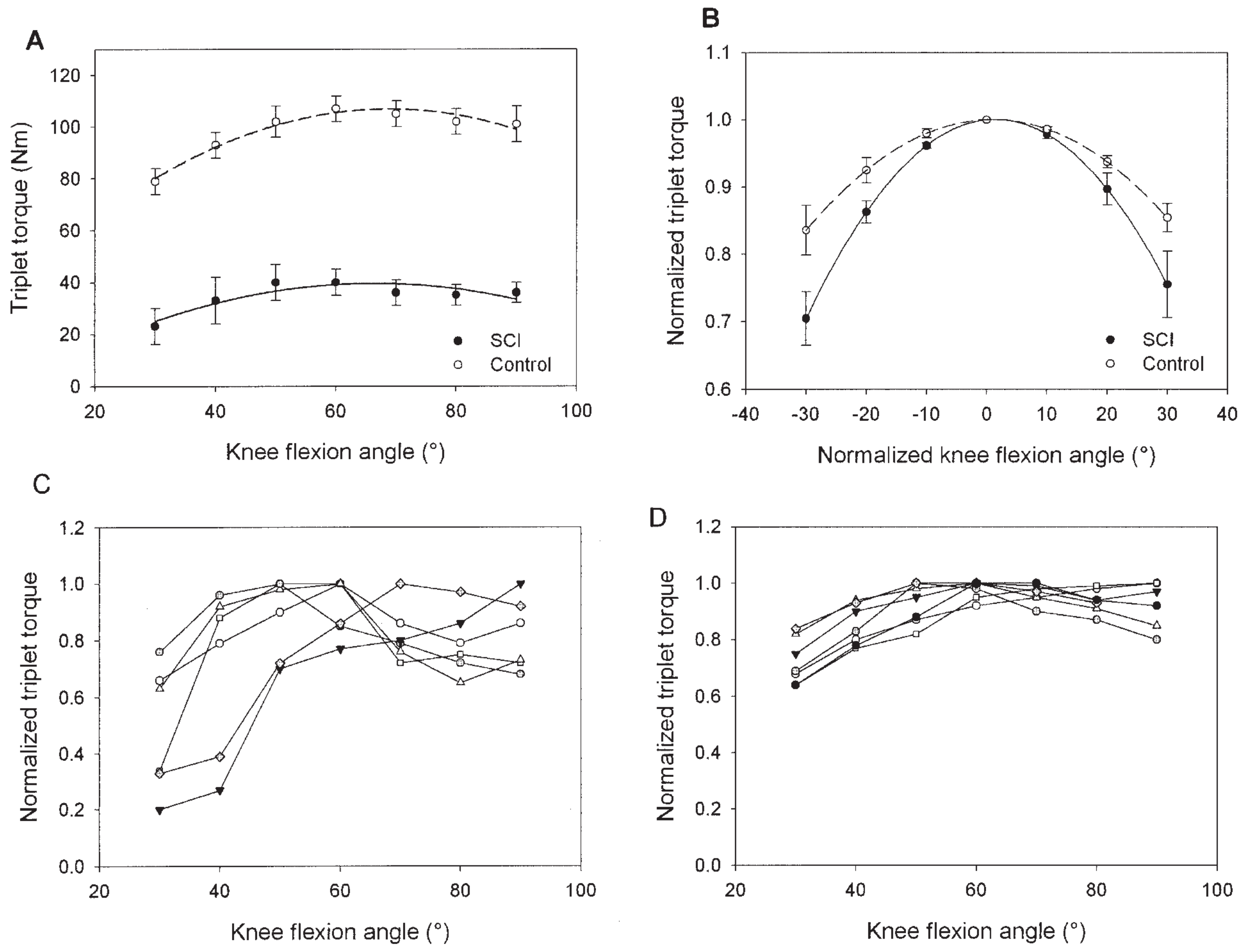

FIGURE 2. Torque–angle relationships of triplet stimulation in six individuals with spinal cord injury (SCI) and seven able-bodied control subjects. **(A)** Average absolute torque responses. **(B)** Torque responses relative to maximum torque plotted against the joint angle relative to optimum. **(C)** Individual normalized torque responses in SCI. **(D)** Individual normalized torque responses in controls. Note that, in **(C)** and **(D)**, data points of individual curves are connected using curve fitting. This was done to more clearly demonstrate the shape of the individual curves. Error bars represent SEM.

control subject, the twitch forces are of similar magnitude. One explanation could be a shortening of the muscle-fiber length since it is known that the force–frequency relationship of a muscle is shifted to the left at longer muscle lengths. This length dependency has been described previously in both animals[9,27] and humans[21] and most likely reflects the length dependency of Ca^{2+} sensitivity in striated muscle.[33] If a shorter quadriceps muscle is measured at the same knee angle as a longer muscle, the shorter muscle would be working at a relatively longer length and would be expected to show a leftward shift in its force–frequency relationship. There are a number of pathologic conditions in which muscles are known to become shorter than normal and it seems likely that this could occur with SCI muscle and might explain our previous observations.

Influence of Knee Angle on Torque Production. The main conclusion to be drawn from the measurements of the angle–torque relationships is that the SCI subjects show a very wide range of curves (Fig. 2); some, as expected, had optimal angles that were shifted to lower angles of flexion (i.e., shorter muscle lengths) but three subjects showed the opposite, with optimum angles greater than those of the control subjects. Reduced muscle activity at a shortened length leads to a shift in the force–length relationship of the muscle to the left (i.e., maximal force production is reached at shorter muscle lengths)[35] due to a reduction in the number of sarcomeres in series. In addition, diseases leading to muscle paralysis, such as stroke,[1] and specific neuromuscular disorders, such as nemaline myopathy,[12] lead to a change in

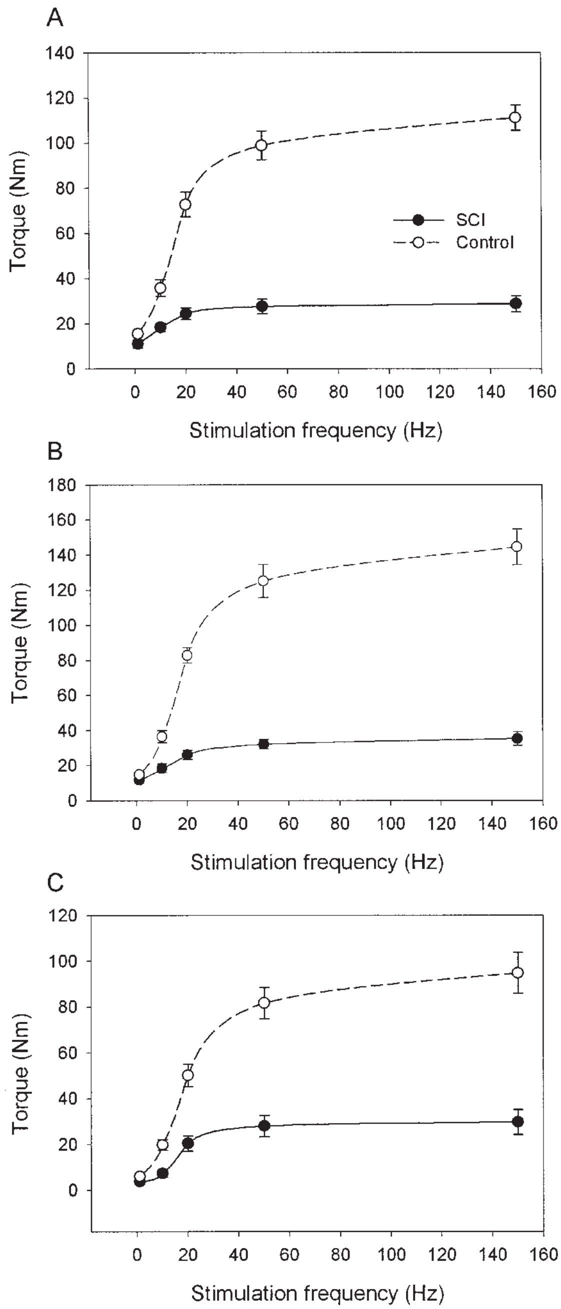

FIGURE 3. Torque–frequency relationships in six individuals with spinal cord injury (SCI) and eight able-bodied control subjects at 90°, corresponding to longer muscle length **(A)** and optimum angle **(B)**, and at 30°, corresponding to shorter muscle length **(C)**. Error bars represent SEM.

the torque–angle relationship of the affected muscles. Consequently, we expected that the optimum for torque production of the knee-extensors would be shifted to lower knee-flexion angles (reflecting shorter muscle length).

Several factors may explain why we did not find such an adaptation. First, individuals with SCI are usually confined to a wheelchair. Consequently, the knee-extensor muscles are lengthened across the knee, and shortened across the hip. Normally, the actual length of the muscle (i.e., the number of sarcomeres in series) is determined by the position in which the muscle is used most. However, since there is hardly any activity present (apart from spasms) in the paralyzed muscles, this regulatory mechanism is likely to be absent in SCI individuals. On average, the optimum angle for torque production was the same in control and SCI muscles. In addition, during in vivo measurements, the mechanical properties of the tendon define, in part, the actual length at which the muscle is operating and therefore affect the torque–angle relationship. Most experiments, using animal models, have shown that immobilization results in decreased stiffness of the

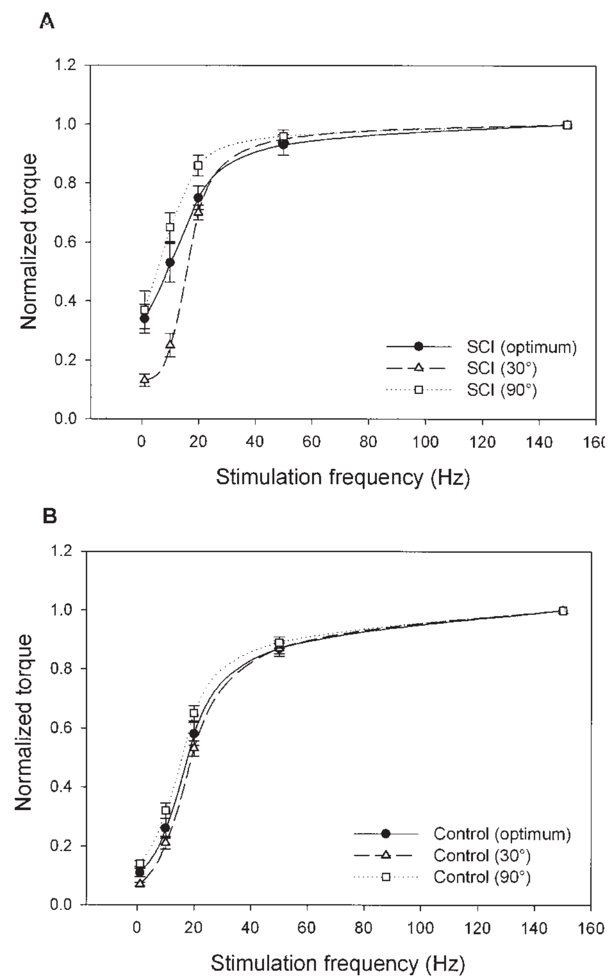

FIGURE 4. Normalized torque–frequency relationships where torques at different stimulation frequencies are expressed relative to maximal stimulation (150 Hz) in six individuals with spinal cord injury (SCI) **(A)** and eight able-bodied control subjects **(B)** at 90°, optimum angle, and 30°. Error bars represent SEM.

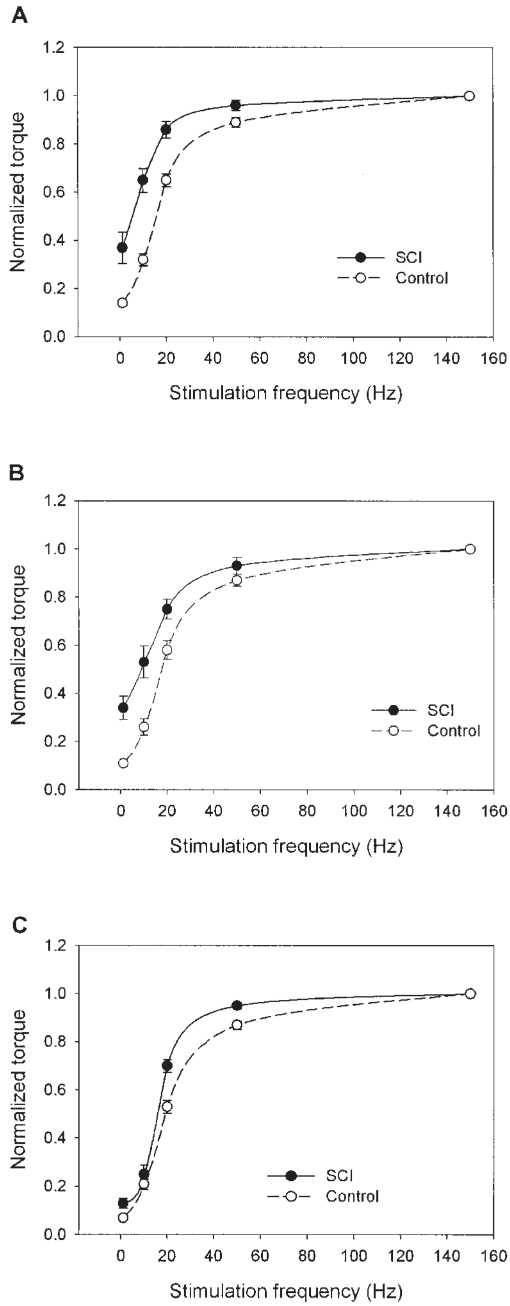

FIGURE 5. Normalized torque–frequency relationships where torques at different stimulation frequencies are expressed relative to maximal stimulation (150 Hz) in six individuals with spinal cord injury (SCI) and eight able-bodied control subjects (Control) at 90° **(A)**, optimum angle **(B)**, and 30° **(C)**. Error bars represent SEM.

tendons[18,29] and human tendons become more compliant after a period of bed-rest[17] or spaceflight.[22] It might be expected that the tendons of individuals with SCI will be more compliant and the actual length at which the muscle is working will be shorter than expected. Such an adaptation would at least partly oppose the shift in the force–length characteristics of the muscle as a result of a loss of sarcomeres. One of these processes may dominate more in one subject than in another, thereby giving rise to the heterogeneity seen among our SCI subjects.

Torque–Frequency Relationship and Effects of Joint Angle. The force (or torque)–frequency relationship has been used to distinguish between "fast" and "slow" muscles, with fast muscles generating less force than slow muscles at low stimulation frequencies.[7,16] Despite this, we[10] and others[26] have demonstrated that the relationships in paralyzed muscles differ in that these intrinsically fast muscles exhibit higher force responses at low stimulation frequencies. There is no clear explanation for this paradoxical finding, but one possibility is that the relative muscle length at which these relationships have been assessed may have confounded the results. For this reason, we investigated the torque–frequency relationships at optimum angle as well as at short (30°) and long (90°) muscle lengths.

We observed a clear effect of joint angle on the torque–frequency relationship, characterized by a shift in the torque–frequency relationships toward lower stimulation frequencies with greater knee flexion (higher muscle length) in both control and SCI subjects (Fig. 4). The SCI muscles produced higher relative torque responses at low stimulation frequencies compared with control muscles at all angles tested, including at the optimum angle where we had hypothesized that the anomalous leftward shift in the force–frequency relationship of the SCI muscles would no longer be seen.

In conclusion, neither of our original hypotheses could be substantiated. There is no evidence of a consistent change in the length of SCI muscles, and the shift in the force–frequency relationship was not an artifact arising from testing the muscle at a relatively long length. We conclude, therefore, that the large twitches seen in stimulated SCI muscle are a real feature of the contractile properties of the muscle. It is of note that a high relative twitch response, similar to that seen in SCI muscles, has been reported in denervated mammalian skeletal muscle.[2,14]

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